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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/525,553 | 02/24/2005 | M.V. Ramana Reddy | 06056-0317US1 | 6059 |

23973 7590 04/13/2007

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| EXAMINER | |
|---|---|
| KUMAR, SHAILENDRA | |
| ART UNIT | PAPER NUMBER |
| 1621 | |

| SHORTENED STATUTORY PERIOD OF RESPONSE | MAIL DATE | DELIVERY MODE |
|---|---|---|
| 3 MONTHS | 04/13/2007 | PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/525,553 | REDDY ET AL. | |
| | Examiner | Art Unit | |
| | SHAILENDRA -. KUMAR | 1621 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *18 January 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *See Continuation Sheet* is/are pending in the application.

4a) Of the above claim(s) *11,15,16,18,19,21,23-34 and 83* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,8,22,24,25,35,43,45-47,50,52,54,56,60,62,68,70,76,77 and 84-89* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/24/05, 4/28/05, 8/23/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims pending in the application are 1, 2, 8, 11, 15, 16, 18, 19, 21-35, 37, 42, 43, 45,-47, 50, 52-54, 56, 60, 62, 68, 70, 76, 77 , 83 and 84-89 .

## DETAILED ACTION

This office action is in response to applicants' communication filed on 1/18/07.

Original claims 1, 2, 8, 11, 15-16, 18-19, 21-35, 37, 42-43, 45, 47, 50, 52-54, 60, 62, 68, 70, 76-77 and 83, and newly added claims 84-89 are pending in this application. The examiner inadvertently omitted claims 52 and 83.

Applicants' response to the examiner's restriction requirement has been noted and agreed upon. Thus as pointed by the applicants, following are the groups:

Group I: Claims 1, 2, 8, 11, 15, 16, 18, 19, 21-35, 43, 45-47, 50, 52, 54, 56, 60, 62, 68, 70, 76, 77 and 83-89.
Group II: Claims 1, 2, 8, 24-26, 35, 43, 45-47, 50, 52, 54, 56, 60, 62, 68, 70, 76, 77, and 84-89.
Group III: Claims 37, 42, and 53.

As discussed on page 70, in the applicants' response, the examiner fully agrees with their comments and interpretation with respect to the restriction requirement.

Applicant's election with traverse of Group I, claims 1, 2, 8, 11, 15, 16, 18, 19, 21-35, 43, 45-47, 50, 52, 54, 56, 60, 62, 68, 70, 76, 77 and 83-89 in the reply filed on 1/18/07 is acknowledged.
The traversal is on the ground(s) that:
The examiner states that unity is lacking because the Groups I-III do not relate to a single general inventive concept under PCT Rule 13.1 because they allegedly lack the same or corresponding special technical features. The examiner states that the reason that Groups I and Groups II lack the same or corresponding technical feature is that Group I compounds are non-heterocyclic whereas group II are heterocyclic. The examiner states that "likewise" Group III lacks the same or corresponding technical feature because it is "drawn to [a] conjugate as against compounds of Groups I and II". MPEP 1893.03(d) reminds examiners that "unity of invention (not restriction) practice is applicable in ... national stage applications submitted under 35 U.S.C. 371." Under the decision in Caterpillar Tractor Co. v. Com'r Pat. & Trademarks, 650 F.Supp. 218 (E.D. Va. 1986), unity of invention must be determined under the provisions of the P.C.T. in a national stage application filed under 35 U.S.C. § 371. Therefore the examiner must make any restriction requirement in accordance with the P.C.T. the P.C.T. rules (specifically Rule 13) and the Administrative Instructions under the P.C.T.
For unity of invention, P.C.T. Rule 13.2 requires "a technical relationship among th[e] inventions involving one or more of the same or corresponding special technical features." (emphasis added). The WIPO Preliminary Examination Guidelines on

Markush practice in the determination of unity of invention point out, "the fact that the alternatives of a Markush group can be differently classified is not, taken alone, considered to be justification for a finding of lack of unity of invention". P.C.T. International Search and Preliminary Examination Guidelines, 10.17(d) (March 25, 2004) (emphasis added).

The compounds of Formula I are clearly a unifying technical feature of Groups I and II. The examiner does not appear to allege otherwise other than by drawing a distinction between "aryl" and "heteroaryl" in the definitions of the rings A and B to conclude that unity of invention is lacking as between compounds where A and B are both aryl (Group I), and those wherein either A or B, or both, are heteroaryl (Group II). Both Groups I and II are, however, drawn to compounds of Formula I, and compositions containing, processes of preparing, and methods of treatment using the compounds. The compounds of Formula I are therefore a unifying technical feature of Groups I and II. The fact that options within the definitions of A and B the options can be differently classified as aryl or heteroaryl does not defeat unity of invention. Aryl and heteroaryl rings, although capable of being differently classified, nevertheless belong to a recognized class, namely aromatic rings. The art recognizes aromatic rings as a single class which includes both carbocyclic and heterocyclic rings, and is defined as encompassing conjugated unsaturated ring systems with 4n+2 pi electrons. As the WIPO guidelines point out, the possibility that the alternatives of a Markush group can be differently classified is not sufficient justification for a finding of lack of unity of invention.
The Formula I structure is also a special technical feature linking Groups I and II with Group III. The structure of the claimed antibody conjugates comprise the structure of Formula I linked to an antibody. The claims to the antibody conjugate are clearly part of the same general inventive concept as the claims to the compounds and their medical use. The inventors have invented the novel compound of Formula I and its therapeutic utility. The antibody conjugates connect the compound of Formula I to an antibody in order to target the delivery of the compound of Formula I to the appropriate site in the body, but, nevertheless, the useful therapeutic utility of the conjugate arises because of the incorporation of Formula I as an essential structural element which imparts the desired activity. The Formula I structure is therefore a technical feature unifying Group III with Groups I and II.
It is respectfully pointed out that the examiner's method of analyzing unity of invention cannot properly determine whether there is unity of the invention because the examiner appears to focus on differences between the Groups, and whether they can be differently classified. The examiner concludes that the Groups lack the same or corresponding technical feature because of
differences between the groups. The WIPO guidelines clearly explain that the possibility of different classification is not sufficient justification for a finding of lack of unity of invention. Further, differences, between the groups, taken alone, are insufficient demonstrate that the inventions lack a common special technical feature - the difference only show that the particular feature defining the difference is not a technical feature

common to the groups. Such differences do not preclude another technical feature from being a common technical feature linking the Groups. . This is not found persuasive because a fact that ring A and B can be different, itself, points out to lack of the same or the corresponding technical feature. Additionally, a reference anticipating one of the compounds wherein A is phenyl and B is phenyl, would not render the compounds wherein A is phenyl and B is heteroaryl etc.

The requirement is still deemed proper and is therefore made FINAL.

Additionally, applicants' election of single disclosed species of example 11, on page 101 is acknowledged. Thus, as pointed out by the applicants, claims 1, 2, 8, 22, 35, 43, 45-47, 50, 52, 54, 56, 62, 68, 70, 76-77 and 84-89 read on the elected species and will be examined to the extent they read on the elected species and closely related species. Thus additionally, claims 11, 15, 16, 18, 19, 21, 23-34 are hereby withdrawn, being drawn to the non elected invention.

***Information Disclosure Statement***

1. The information disclosure statement (IDS) submitted on 2/24/05, 4/28/05 and 8/23/06 are in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statements have been considered by the examiner.

***Claim Rejections - 35 USC § 112***

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 43, 45-47, 50, 52, 54, 56, 62, 68, 70, 76-77, 84-89 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a

way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. § 112, first paragraph, have been described. They are:

1. the nature of the invention,
2. the state of the prior art,
3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,
5. the presence or absence of working examples,
6. the breadth of the claims,
7. the quantity of experimentation needed, and
8. the level of the skill in the art.

***The nature of the invention***

The nature of the invention is the method of treating an individual for a proliferative disorder comprising administering to said individual an effective amount of at least one compound according to claim 43, or a salt thereof. This includes all types of cancer.

***The state of the prior art and the predictability or lack thereof in the art***

The state of the prior art is that it involves screening *in vitro* and *in vivo* to determine which compounds exhibit the desired pharmacological activities (i.e. what compounds can treat which specific disease). There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic or preventive regimen on its face.

The instant claimed invention is highly unpredictable as discussed below:

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In re Fisher, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. In the instant case, the instant claimed invention is highly unpredictable since one skilled in the art would recognize that in regards to therapeutic effects of disorders, whether or not the disease is effected by cytoprotective agents.

***The breadth of the claims***

The breadth of the claims is the method of treating an individual for a proliferative disorder comprising administering to said individual an effective amount of at least one compound according to formula of claim 43.

***The quantity of experimentation needed***

The quantity of experimentation needed is undue experimentation. One of skill in the art would need to determine what kind of cancer out of all kinds of cancer would be benefited by the administration of the instant claimed compounds.

***The level of the skill in the art***

The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by in vitro and in vivo screening to determine which compounds exhibit the desired pharmacological activity and which diseases would benefit from this activity.

Thus, the specification fails to provide sufficient support of the broad use of the compound of the formula of claim 43 inhibiting the proliferation of the various cancer cells. As a result necessitating one of skill to perform an exhaustive search for which disorders can be treated by what compounds of formula (I)3 in order to practice the claimed invention.

Genentech Inc. v. Novo Nordisk A/S (CA FC) 42 USPQ2d 1001 , states that " a patent is not a hunting license. It is not a reward for search , but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the Wands factors and In re Fisher (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in undue experimentation to test which disorders can be treated by the compound encompassed in the instant claims, with no assurance of success.

***Claim Rejections - 35 USC § 103***

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 1, 2, 8, 22 and 35 are rejected under 35 U.S.C. 103(a) as being unpatentable over JP 2001-139550.

JP'550 teaches structurally similar compounds and composition as claimed herein, see for example abstract, formula (I), wherein, Ar1 and A can be phenyl, both substituted, Z can be O, n can be 1, and R can be H. Also see compounds on page 15, especially, compound Ia-64, Ia -65 and I-63. The difference between the reference and herein claimed compounds and composition is that the most of the compounds made in the reference has been proviso out in herein.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to obtain compounds within the generic disclosure of the reference, because they are structurally so similar to those claimed herein, with the

reasonable expectation of achieving composition for using in the method of arteriosclerosis, absent evidence to the contrary. Note compounds Ia-68 and Ia-64, wherein, equivalence of OH and OMe are expressly taught.

8. Claims 24-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Abraham(US 5,705,521).

Abraham teaches similar process of preparing structurally similar compounds as claimed herein, see for example, Fig 15, Fig 16, Fig 25. The difference between the reference and herein claimed process is that the reference has not made compounds claimed herein.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use the process of Abraham by starting with structurally similar starting material as claimed herein, because the process per se is no more than an analogous process, with the reasonable expectation of achieving a successful product similar to those claimed herein, absent evidence to the contrary.

9. **The elected species appears to be free of prior art and is allowable. Claims readable on the elected species and closely related compounds would be allowed, along with the composition and corresponding process claims.**

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to SHAILENDRA -. KUMAR whose telephone number is (571)272-0640. The examiner can normally be reached on Mon-Thur 8:00-5:30, Alt Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman Page can be reached on (571)272-0602. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

SHAILENDRA - KUMAR
Primary Examiner
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S.Kumar
4/9/07